

# Electronic Information Disclosure Statement

Composite blastocysts (CBs) from  
aggregates of dissociated cells of  
non-viable pre-embryos



RECEIVED

JUN 24 2002

TECH CENTER 1600/2900

Application:



10/036581

Confirmation:

4092

Applicant(s):

Mina Alikani

Docket Number:

Group Art Unit:

Examiner:

search string:

( 5541081 or 5843780 or 6200806 or 6280718 or 6132952 ).pn.

## US Patent Documents

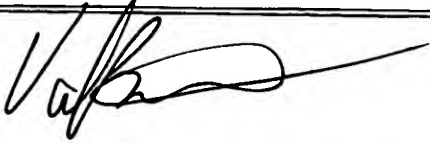
Note: Applicant is not required to submit a paper copy of cited US Patent Documents

init	Citation No.	Patent Number	Date	Bar Code	Patentee	Class	Subclass
VB	P01	5541081	1996-07-30		Hardy et al.	435	24
VB	P02	5843780	1998-12-01		Thomson	435	363
VB	P03	6200806	2001-03-13		Thomson	435	366
VB	P04	6280718	2001-08-28		Kaufman et al.	435	363
VB	P05	6132952	2000-10-17		Cohen et al.	435	2

*Albert*

01/21/04

## Signature

Examiner Name	Date
	8/21/04

## Information Disclosure Statement by Applicant

### U.S. Patent Documents

- ✓ 5061620 Oct., 1991 Tsukamoto et al. 435/7.
- ✓ 5166065 Nov., 1992 Williams et al. 435/325.
- ✓ 5340740 Aug., 1994 Petite et al. 435/325.
- ✓ 5449620 Sep., 1995 Khillan 435/325.
- ✓ 5453357 Sep., 1995 Hogan 435/7.
- ✓ 5523226 Jun., 1996 Wheeler 435/325.
- ✓ 5589376 Dec., 1996 Anderson et al. 435/325.
- ✓ 591625 Jan., 1997 Gerson et al. 435/325.
- ✓ 5635386 Jun., 1997 Palsson et al. 435/372.
- ✓ 5843780 Dec., 1998 Thomson 435/363.
- ✓ 5914268 Jun., 1999 Keller et al. 435/325.
- ✓ 6132952 Oct., 2000 Cohen et al. 435/2.
- ✓ 6200806 Mar., 2001 Thomson 435/366.
- ~~✓ 6289718 Aug., 2001 Kaufman et al. 424/93.1, 435/363.~~

COPY OF PAPERS  
ORIGINALLY FILED

1c997 U.S. PTO  
10/036581  
11/06/01

### Foreign Patent Documents

- ✓ 94/03585 Feb., 1994 WO.
- ✓ 98/07841 Feb., 1998 WO.
- ✓ 00/32140, Nov 98 WO
- ✓ 00/0012682 Mar., 2000 WO
- ✓ 01/0134776 May, 2001 WO
- ✓ 01/0162899 Aug., 2001 WO

### Other References:

- ✓ National Institutes of Health Guidelines for Research Using Human Pluripotent Stem Cells. National Institutes of Health, [www.nih.gov/news/stemcell/stemcellguidelines.htm](http://www.nih.gov/news/stemcell/stemcellguidelines.htm), pp. 1-13, Nov. 1, 2000, 65 FR 69951.

Fletcher L.

- ✓ US Stem cell policy comes under fire.  
Nature Biotechnology, 19: 893-894, 2001.

Tarkowski AK and Wroblewska J.

- ✓ Development of blastomeres of mouse eggs isolated at the 4- and 8-cell stage  
J Embryology and Experimental morphology, 18(1): 155-80, 1967.

Willadsen SM.

- ✓ Cloning of sheep and cow embryos.  
Genome, 31(2):956-962, 1989.

*Valho* 01/24/04

- VB Willadsen SM.  
Nuclear transplantation in sheep embryos.  
Nature, 320:63-65, 1986.
- VB Fehilly CB, Willadsen SM.  
Embryo manipulation in farm animals.  
Oxf Rev Reprod Biol., 8: 379-413, 1986.
- VB Fehilly CB, Willadsen SM, Dain AR, Tucker EM.  
Cytogenetic and blood group studies of sheep/goat chimaeras.  
J Reprod Fertil., 74(1): 215-21, 1985.
- VB Willadsen SM, Godke RA.  
A simple procedure for the production of identical sheep twins.  
Vet Rec., 114(10): 240-3, 1984.
- VB Fehilly CB, Willadsen SM, Tucker EM.  
Interspecific chimaerism between sheep and goat.  
Nature. 1984 Feb 16-22;307(5952):634-6.
- VB Fehilly CB, Willadsen SM, Tucker EM.  
Experimental chimaerism in sheep.  
J Reprod Fertil., 70(1):347-51, 1984.
- VB Willadsen SM.  
The development capacity of blastomeres from 4- and 8-cell sheep embryos.  
J Embryol Exp Morphol., 65:165-72, 1981.
- VB Willadsen SM, Polge C.  
Attempts to produce monozygotic quadruplets in cattle by blastomere separation.  
Vet Rec., 108(10): 211-3, 1981.
- VB Willadsen SM.  
The viability of early cleavage stages containing half the normal number of blastomeres in the sheep.  
J Reprod Fertil., 59(2):357-62, 1980.
- VB Willadsen SM.  
A method for culture of micromanipulated sheep embryos and its use to produce monozygotic twins.  
Nature, 277:298-300, 1979.

*Valh* 01/24/04

- ✓<sup>13</sup> Barritt J, Willadsen S, Brenner C, Cohen J.  
Cytoplasmic transfer in assisted reproduction.  
Hum Reprod Update. 2001 Jul-Aug;7(4):428-35.
- ✓<sup>13</sup> Willadsen S, Levron J, Munne S, Schimmel T, Marquez C, Scott R, Cohen J.  
Rapid visualization of metaphase chromosomes in single human blastomeres after fusion with in-vitro matured bovine eggs.  
Hum Reprod. 1999 Feb;14(2):470-5.
- ✓<sup>13</sup> Levron J, Willadsen SM, Shimmel T, Cohen J.  
Cryopreservation of activated mouse oocytes and zygote reconstitution after thaw.  
Hum Reprod. 1998 Dec;13 Suppl 4:109-16.
- ✓<sup>13</sup> Sandalinas M, Sadowy S, Alikani M, Calderon G, Cohen J, Munne S.  
Developmental ability of chromosomally abnormal human embryos to develop to the blastocyst stage. Hum Reprod. 2001 Sep;16(9):1954-8.
- ✓<sup>13</sup> Alikani M, Calderon G, Tomkin G, Garrisi J, Kokot M, Cohen J.  
Cleavage anomalies in early human embryos and survival after prolonged culture in-vitro.  
Hum Reprod., 15(12):2634-43, 2000.
- ✓<sup>13</sup> Cao W, Brenner CA, Alikani M, Cohen J, Warner CM.  
Search for a human homologue of the mouse Ped gene.  
Mol Hum Reprod., 5(6):541-7, 1999.
- ✓<sup>13</sup> Alikani M, Cohen J, Tomkin G, Garrisi GJ, Mack C, Scott RT.  
Human embryo fragmentation in vitro and its implications for pregnancy and implantation.  
Fertil Steril., 71(5):836-42, 1999.
- ✓<sup>13</sup> Warner CM, Cao W, Exley GE, McElhinny AS, Alikani M, Cohen J, Scott RT, Brenner CA.  
Genetic regulation of egg and embryo survival.  
Hum Reprod., 13 Suppl 3:178-90; discussion 191-6, 1998.
- ✓<sup>13</sup> Cohen J, Alikani M, Garrisi JG, Willadsen S.  
Micromanipulation of human gametes and embryos: ooplasmic donation at fertilization.  
Hum Reprod Update. 1998 Mar-Apr;4(2):195-6.
- ✓<sup>13</sup> Munne S, Marquez C, Reing A, Garrisi J, Alikani M.  
Chromosome abnormalities in embryos obtained after conventional in vitro fertilization and intracytoplasmic sperm injection.

Valbe 04/21/04

Fertil Steril. 1998 May;69(5):904-8.

✓3 Cohen J, Scott R, Alikani M, Schimmel T, Munne S, Levron J, Wu L, Brenner C, Warner C, Willadsen S.

Ooplasmic transfer in mature human oocytes.  
Mol Hum Reprod. 1998 Mar;4(3):269-80.

✓3 Kligman I, Benadiva C, Alikani M, Munne S.

The presence of multinucleated blastomeres in human embryos is correlated with chromosomal abnormalities.  
Hum Reprod. 1996 Jul;11(7):1492-8.

✓3 Alikani M, Palermo G, Adler A, Bertoli M, Blake M, Cohen J.  
Intracytoplasmic sperm injection in dysmorphic human oocytes.  
Zygote. 1995 Nov;3(4):283-8.

✓3 Munne S, Alikani M, Tomkin G, Grifo J, Cohen J.  
Embryo morphology, developmental rates, and maternal age are correlated with chromosome abnormalities.  
Fertil Steril. 1995 Aug;64(2):382-91.

✓3 Alikani M, Cohen J, Palermo GD.  
Enhancement of fertilization by micromanipulation.  
Curr Opin Obstet Gynecol. 1995 Jun;7(3):182-7.

✓3 Sultan KM, Munne S, Palermo GD, Alikani M, Cohen J.  
Chromosomal status of uni-pronuclear human zygotes following in-vitro fertilization and intracytoplasmic sperm injection.  
Hum Reprod. 1995 Jan;10(1):132-6.

✓3 Alikani M, Noyes N, Cohen J, Rosenwaks Z.  
Monozygotic twinning in the human is associated with the zona pellucida architecture.  
Hum Reprod. 1994 Jul;9(7):1318-21.

✓3 Grifo JA, Tang YX, Munne S, Alikani M, Cohen J, Rosenwaks Z.  
Healthy deliveries from biopsied human embryos.  
Hum Reprod. 1994 May;9(5):912-6.

✓3 Cohen J, Alikani M, Liu HC, Rosenwaks Z.  
Rescue of human embryos by micromanipulation.  
Baillieres Clin Obstet Gynaecol. 1994 Mar;8(1):95-116. Review.

✓3 Munne S, Alikani M, Cohen J.  
Monospermic polyploidy and atypical embryo morphology.  
Hum Reprod. 1994 Mar;9(3):506-10

Valh 01/21/04

V3

Cohen J, Schattman G, Suzman M, Adler A, Alikani M, Rosenwaks Z.  
Micromanipulating human gametes.  
Reprod Fertil Dev. 1994;6(1):69-81; discussion 81-3.

Liu HC, Cohen J, Alikani M, Noyes N, Rosenwaks Z.  
Assisted hatching facilitates earlier implantation.  
Fertil Steril. 1993 Nov;60(5):871-5.

Alikani M, Olivennes F, Cohen J.  
Microsurgical correction of partially degenerate mouse embryos promotes hatching and restores their viability.  
Hum Reprod. 1993 Oct;8(10):1723-8.

Alikani M.  
Micromanipulation of human gametes for assisted fertilization.  
Curr Opin Obstet Gynecol. 1993 Oct;5(5):594-9. Review.

Neev J, Gonzalez A, Licciardi F, Alikani M, Tadir Y, Berns M, Cohen J.  
Opening of the mouse zona pellucida by laser without a micromanipulator.  
Hum Reprod. 1993 Jun;8(6):939-44.

Alikani M, Cohen J.  
Micromanipulation of cleaved embryos cultured in protein-free medium: a mouse model for assisted hatching.  
J Exp Zool. 1992 Oct 1;263(4):458-63.

Cohen J, Alikani M, Reing AM, Ferrara TA, Trowbridge J, Tucker M.  
Selective assisted hatching of human embryos.  
Ann Acad Med Singapore. 1992 Jul;21(4):565-70.

Cohen J, Alikani M, Trowbridge J, Rosenwaks Z.  
Implantation enhancement by selective assisted hatching using zona drilling of human embryos with poor prognosis.  
Hum Reprod. 1992 May;7(5):685-91.

Cohen J, Alikani M, Malter HE, Adler A, Talansky BE, Rosenwaks Z.  
Partial zona dissection or subzonal sperm insertion: microsurgical fertilization alternatives based on evaluation of sperm and embryo morphology.  
Fertil Steril. 1991 Oct;56(4):696-706.

V3

Pike IL, Alikani M.  
Time-dependent loss of developmental potential when two-celled mouse embryos were retained in culture in excised oviducts.  
Ann N Y Acad Sci. 1988;541:419-23.

Val B. J. 01/21/04

- ✓B Cohen J, Gilligan A, Willadsen S.  
Culture and quality control of embryos.  
Hum Reprod. 1998 Jun;13 Suppl 3:137-44; discussion 145-7.
- ✓B Cohen J, Scott R, Schimmel T, Levron J, Willadsen S.  
Birth of infant after transfer of anucleate donor oocyte cytoplasm into recipient eggs.  
Lancet. 1997 Jul 19;350(9072):186-7.
- ✓B Levron J, Willadsen S, Bertoli M, Cohen J.  
The development of mouse zygotes after fusion with synchronous and asynchronous cytoplasm.  
Hum Reprod. 1996 Jun;11(6):1287-92.
- ✓B Levron J, Willadsen S, Munne S, Cohen J.  
Formation of male pronuclei in partitioned human oocytes.  
Biol Reprod. 1995 Jul;53(1):209-13.
- ✓B Levron J, Munne S, Willadsen S, Rosenwaks Z, Cohen J.  
Male and female genomes associated in a single pronucleus in human zygotes.  
Biol Reprod. 1995 Mar;52(3):653-7.
- ✓B Cohen J., Malter, C Fehilly, G Wright, C Elsner, H Kort, J Massey (1988)  
Implantation of embryos after partial opening of the oocyte zona pellucida to facilitate sperm penetration.  
Lancet, 1988 ii:162.
- ✓B Cohen J, HE Malter, C Elsner, H Kort, J Massey, MP Mayer (1989)  
Partial zona dissection of human oocytes when failure of zona pellucida penetration is anticipated.  
Hum Reprod 4:435-442.
- ✓B Malter HE, J Cohen (1989) Partial zona dissection of the human oocyte: a nontraumatic method using micromanipulation to assist zona pellucida penetration.  
Fertil Steril 51:139-148.
- ✓B Malter HE, J Cohen (1989) Embryonic development after microsurgical repair of polyspermic human zygotes.  
Fertil Steril 52:373-380.
- ✓B Malter HE, J Cohen (1989) Blastocyst formation and hatching in vitro following zona drilling of mouse and human embryos.  
Gamete Res 24:67-80.

*Handwritten signature* 01/21/04



VB Cohen J, C Elsner, H Kort, H Malter, J Massey, MP Maye, K Wiemer (1990) Impairment of the hatching process following IVF in the human and improvement of implantation by assisting hatching using micromanipulation.  
Hum Reprod 5:7-13.

VB Wiker S, H Malter, G Wright, J Cohen (1990) Recognition of paternal pronuclei in human zygotes.  
J In Vitro Fertil Emb Transfer 7:33-37

VB J.Nicos and R.L. Gardner  
Heterogeneous differentiation of external cells in individual isolated mouse inner cell masses in culture.  
Embryol. Exp. Morphol.; 80:225-240,1984.

Andrews, P. et al.  
Cell lines from human germ cell tumours.  
Teratocarcinoms and Embryonic Stem Cells; A Practical Approach, Oxford: IRL Press, Ch. 8:207-248 (1987).

Andrews, P., et al.  
Pluripotent Embryonal Carcinoma Clones Derived from the Human Teratocarcinoma Cell Line Tera-2.  
Lab. Invest., 50(2):147-162 (1984).

Bongso, A., et al.,  
Isolation and culture of inner cell mass cells from human blastocysts  
Human Reprod., 9(1):2110-2117 (1994).

VB Bongso, A., et al., "The Growth of Inner Cell Mass Cells from Human Blastocysts," Theriogenology, 41:167 (1994).

VB Doetschman, T., et al.  
Establishment Of Hamster Blastocyst-Derived Embryonic Stem (ES) Cells  
Developmental Biology, 127:224-227 (1988).

VB Doetschman, T., et al.  
The in vitro development of blastocyst-derived embryonic stem cell lines: formation of visceral yolk sac, blood islands and myocardium, J. Embryol. Exp. Morph., 87:27-45 (1985).

VB Evans, M., et al.  
Establishment in culture of pluripotential cells from mouse embryos,  
Nature, 292:154-156 (1981).

ValB 01/21/04

Evans, M., et al.  
Derivation and Preliminary Characterization of Pluripotent Cell Lines  
from Porcine and Bovine Blastocysts  
Theriogenology, 33(1):125-128 (1990).

Giles, J., et al.  
Pluripotency of Cultured Rabbit Inner Cell Mass Cells Detected by  
Isozyme Analysis and Eye Pigmentation of Fetuses Following Injection  
into Blastocysts or Morulae.  
Mol. Reprod. Dev., 36:130-138 (1993).

Graves, K., et al.,  
Derivation and Characterization of Putative Pluripotential Embryonic  
Stem Cells from Preimplantation Rabbit Embryos.  
Mol. Reprod. Dev., 36:424-433 (1993).

✓ Notarianni, E., et al.  
Maintenance and differentiation in culture of pluripotential embryonic cell  
lines from pig blastocysts.  
J. Reprod. Fert. Suppl., 41:51-56 (1990).

✓ Notarianni, E., et al.  
Derivation Of Pluripotent, Embryonic Cell Lines From The Pig And  
Sheep.  
J. Rep. & Fert. 43 255-260 (1991).

✓ Piedrahita, et al.,  
On The Isolation Of Embryonic Stem Cells: Comparative Behavior Of  
Murine, Porcine And Ovine Embryos  
Theriogenology, 34(5):879-901 (1990).

✓ Rossant, J., et al.  
The relationship between embryonic, embryonal carcinoma and embryo-  
derived stem cells.  
Cell Diff., 15:155-161 (1984).

✓ Seshagiri, P., et al.  
Non-Surgical Uterine Flushing for the Recovery of Preimplantation  
Embryos in Rhesus Monkeys: Lack of Seasonal Infertility.  
Am. J. Primatol., 29:81-91 (1993).

✓ Strojek, R. et al.  
A Method For Cultivating Morphologically Undifferentiated Embryonic  
Stem Cells From Porcine Blastocysts.  
Theriogenology 33 901-913 (1990).

*Val* 01/21/04

- ✓<sup>b</sup> Sukoyan, M., et al.  
Isolation and Cultivation of Blastocyst-derived Stem Cell Lines from American Mink (*Mustela vison*)  
*Mol. Reprod. Dev.*, 33:418-431 (1992).
- ✓<sub>B</sub> Sukoyan, M., et al.  
Embryonic Stem Cells Derived from Morulae, Inner Cell Mass, and Blastocysts of Mink: Comparisons of Their Pluripotencies  
*Mol. Reprod. Deve.*, 36:148-158 (1993).
- ✓<sub>B</sub> Talbot, et al.  
Culturing The EpiBlast Cells Of The Pig Blastocyst  
*In Vitro Cell. Dev. Bio.*, 29(A):543-554 (1993).
- ✓<sub>B</sub> Thomson, J., et al.  
Nonsurgical uterine stage preimplantation embryo collection from the common marmoset  
*J. Med. Primatol.*, 23:333-336 (1994).
- ✓<sub>B</sub> Thomson, James A., et al.  
Pluripotent Cell Lines Derived from Common Marmoset (*Callithrix jacchus*) Blastocysts.  
*Biology of Reproduction*, 55:254-259 (1996).
- ✓<sub>B</sub> Ware, et al.  
Development Of Embryonic Stem Cell Lines From Farm Animals  
*Biol. Reprod.*, 38(Suppl. 1):129 (1988).
- ✓<sub>B</sub> Thomson et al. Embryonic Stem Cell Lines Derived from Human Blastocysts.  
*Science*, vol. 282, pp. 1145-1147, Nov. 6, 1998.
- ✓<sub>B</sub> Cruz et al. Origin of Embryonic and Extraembryonic Cell Lineages in Mammalian Embryos.  
*Current Communications*, vol. 4, pp. 147-204, 1991.
- ✓<sub>B</sub> Nichols et al.  
Establishment of germ-line-competent embryonic stem (ES) cells using differentiation inhibiting activity.  
*Development*, vol. 110, pp. 1341-1348, 1990.
- ✓<sub>B</sub> Thomson J. et al., Embryonic Stem Cell Lines Derived From Human Blastocysts.  
*Science*, 282: 1145 -1147 (1998).

Valle 0